CBI Chemistry-Biology Interface:
A multi-disciplinary graduate program
at the interface between chemistry and biology

Fall 2020

ZOOM LINK: If you are not affiliated with the University of Delaware, please contact the CBI Coordinator, Stephanie Bergwall at bergwall@udel.edu, if you would like to attend a seminar

Date	Speaker	Title
September 2	Student Research presentation	**Stephen Hyland**: **"Investigation of MurJ as a Potential Antibiotic Target through Utilization of Electrophilic MurNAc Derivatives"**
September 4	**Dr. Ellen Sletten** Assistant Professor Chemistry & Biochemistry University of California, Los Angeles, UCLA - The Sletten Group	
September 9	**Dr. Salil Lachke** Professor and Associate Chair Alumni Distinguished Early Career Professor of Biology Department of Biological Sciences Dr. Lachke's Webpage	**"Post-transcriptional Gene Regulatory Networks in Eye Development and Disease"**
September 16	**Jim Melnyck, PhD** Postdoctoral Fellow University of California, San Francisco, UCSF	**"Targeting a Splicing-mediated Resistance Mechanism in Prostate Cancer"**
September 23	**Professor Yimon Aye** Faculty at EPFL (École polytechnique fédérale de Lausanne) Laboratory of electrophiles and genome operation (LEAGO)	**"Within our control? Illuminating how ephemeral electrophiles rewire cell decision-making processes"**

September 30	**Dr. Avi Schroeder**, Associate Professor of Chemical Engineering, Technion Adjunct Associate Professor of Biomedical Engineering, Technion Laboratory for Targeted Drug Delivery and Personalized Medicine Technologies, Head Technion - Israel Institute of Technology, Haifa 32000, Israel	**"Barcoded Nanoparticles for Precision Cancer Medicine: Effects of tumor type and patient sex on anticancer efficacy"**
October 7	Post doc panel	**Jodi Kraus; Kristen DeMeester; Walter Drake; Nathan McDonald; Rachel Riley**
October 14	Molly C. Sutherland, PhD Assistant Professor Department of Biological Sciences	**"Cytochrome c biogenesis in bacteria"**
October 21	Lab rotation talks	**Eli Learn; Stephanie Tsang; Ellie Meck; Teresa Cruz**
October 28	**PUMPKIN DECORATING CONTEST**	
November 4	Adv student talks	**Erica Green** **Alex Mitkas**
November 11	Adv student talks	**Nate Hamaker** **Mike Clupper**
November 18	Adv student talks	**Ophelia Ukaegbu** **Allyson Dang**
November 25	THANKSGIVING	
December 2	RCR - lab notebook panel	**Emily Day** **Mary Watson**

December 9	Poster Session	Open to all CBI students. Mandatory for 1st year: **Eli Learn; Stephanie Tsang; Ellie Meck; Teresa Cruz**

Seminars are on Wednesday noon-1 pm, virtual, Zoom link:
https://udel.zoom.us/j/99512595421?pwd=K1VhRXFpaGtubTUwUDRkYXlQTHhUQT09

Dr. Yimon Aye Abstract:

Abstract: Precisely timed and spatially regulated electrophilic chemical signals are slowly being implicated as bona fide signaling events in numerous cells. However, modeling these low-stoichiometry signaling events and defining the precise biological impacts of localized signals under physiologic conditions has proven to be highly challenging[1]. The first half of the presentation will spotlight a unique set of proximity-directed chemical biology tools that enables interrogation into functional consequences of specific redox-linked events: namely, T-REX™ precision electrophile delivery and G-REX™ electrophile-ligandability profiling in living systems[2], and how using these technologies have enabled us to identify bona fide "*first responders*" that interact with native signaling electrophiles under close to endogenous redox signaling conditions (i.e., "k_{cat}/K_m"-like). Our data show that these first responders lie at nexuses between electrophile- and canonical-signaling pathways. Thus, these proteins translate information encoded by electrophiles to phosphate or ubiquitin to reroute signaling pathway flux, even at the organismal level. The second half of the presentation will relate to our latest data of unique relevance to medicinal chemistry research: i.e., our new ability to discover and functionally decipher precision electrophile signaling mechanisms[3] toward targeted therapeutics and novel target discovery[4]. Here, I will discuss successful small-molecule targeting of otherwise hard-to-treat *pten*-null triple-negative breast cancers in cells and xenograft mouse tumor models[5], guided by our recent identification of protein-isoform-specific native electrophilic metabolite sensing in living cells and larval zebrafish[6].

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[1] https://www.ncbi.nlm.nih.gov/pubmed/30913473 Genie in a Bottle: Controlled Release Helps Tame Natural Polypharmacology? *Current Opinion in Chemical Biology* **2019** *51* 48 (with Long et al.)

[2] https://www.ncbi.nlm.nih.gov/pubmed/30765181 Interrogating Precision Electrophile Signaling, *Trends in Biochemical Sciences (Invited Technology Corner)* 2019 *44* 380 (with Poganik et al.)

[3] **2020** (in peer review) (with Zhao et al.)

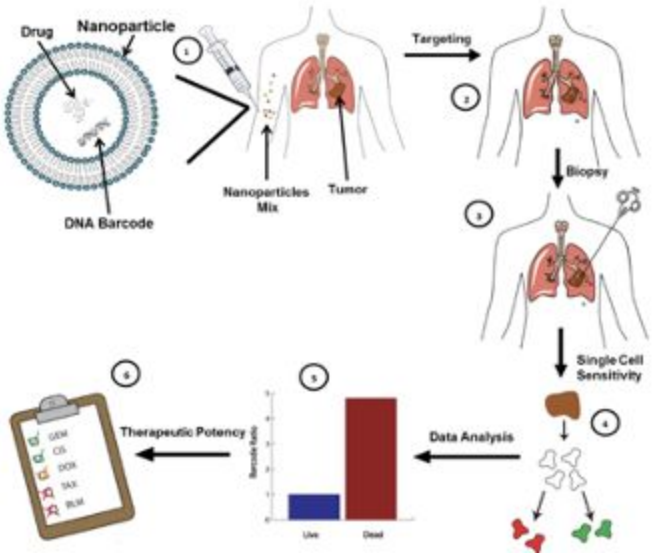
[4] https://www.ncbi.nlm.nih.gov/pubmed/28648380 Privileged Electrophile Sensors: A Resource for Covalent Drug Development, *Cell Chemical Biology (Invited Perspective)* **2017** *24* 787 (with Long)

[5] (i) Liu, Long, and Aye, **2018** PCT Patent filed; (ii) https://pubmed.ncbi.nlm.nih.gov/32607436/ Precision Targeting of *pten*-Null Triple-Negative Breast Tumors Guided by Electrophilic Metabolite Sensing *ACS Central Science* **2020** (with Liu et al.)

[6] https://www.ncbi.nlm.nih.gov/pubmed/28114274 Akt3 is A Privileged First Responder in Isozyme-Specific Electrophile Response, *Nature Chemical Biology* **2017** *13* 333 (with Long and Parvez et al.)

Dr. Avi Schroeder Abstract:

Medicine is taking its first steps towards patient-specific cancer care. Nanoparticles have many potential benefits for treating cancer, including the ability to transport complex molecular cargoes including siRNA and protein, as well as targeting to specific cell populations. The talk will discuss 'barcoded nanoparticles' that target sites of cancer where they perform a programmed therapeutic task. Specifically, liposomes that diagnose the tumor and metastasis for their sensitivity to different medications, providing patient-specific drug activity information that can be used to improve the medication choice. The talk will also describe how liposomes can be used for degrading the pancreatic stroma to allow subsequent drug penetration into pancreatic adenocarcinoma, and how nanoparticle' biodistribution and anti-cancer efficacy is impacted by patient' sex and more specifically, the menstrual cycle. The evolution of drug delivery systems into *synthetic cells*, programmed nanoparticles that have an autonomous capacity to synthesize diagnostic and therapeutic proteins inside the body, and their promise for treating cancer and immunotherapy, will be discussed.



References:

1) Theranostic barcoded nanoparticles for personalized cancer medicine, Yaari et al. ***Nature Communications*****,** 2016, 7, 13325

2) Synthetic Cells Synthesize Therapeutic Proteins inside Tumors, Krinsky et al., ***Advanced Healthcare Materials,*** 2017

3) Collagenase nanoparticles enhance the penetration of drugs into pancreatic tumors, Zinger et al., ***ACS Nano,*** 2019